

Docket No.: C1039.70079US00

(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:

Arthur M. Krieg

Serial No.:

10/627,413

Confirmation No.:

3204

Filed:

July 25, 2003

For:

METHODS FOR TREATING AND PREVENTING INFECTIOUS

DISEASE

Examiner:

Le, Emily M.

Art Unit:

1648

Certificate of Mailing Under 37 CFR 1.8(a)

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the U.S. Postal Service on the date shown below with sufficient postage as First Class Mail, in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: March 30, 2007

<u>PETITION UNDER 37 C.F.R. § 1.181 AND §1.182</u>

MAIL STOP PETITION Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Dear Sir:

The information disclosure statement filed by Applicant has been objected to under 37 CFR 1.56(b) and not considered. The Examiner has quoted CFR 1.56 (b) and then concluded that the information provided in the 46 references that she did review "do not compel a conclusion that a claim is unpatentable." Accordingly, she concluded that "the submission is not in compliance with 37 CFR 1.56 and 1.98."

Applicants assert that they have complied with their duty of disclosure as outlined in the MPEP §609 and §2001- 2004 and in compliance with 35 C.F.R. §1.56, §1.97 and §1.98. Applicants present a clean copy of the IDS previously submitted for review by the Examiner (omitting those references that have already been considered) with a Petition for review of these references under 37 C.F.R. §1.181 and §1.182. The clean copy is updated with the format requirements now in place

under 37 CFR 1.98(a)(1). Applicants request that these references be reviewed by the Examiner and be granted the date of submission of the original filed IDS.

Applicant's strongly disagree with the Examiner's refusal to consider the IDS. Initially, Applicants point out that they are in agreement that the references "do not compel a conclusion that a claim is unpatentable." If Applicants had information that compelled a conclusion that a claim was unpatentable, Applicants would not pursue such a claim.

The position taken by the Examiner in refusing to review the references set forth in the IDS is inconsistent with the Patent Office policy of requesting information. For instance, "once the minimum requirements of 37 CFR 1.97 and 37 CFR 1.98 are met, the examiner has an obligation to consider the information." (MPEP 609, emphasis added). Additionally, the Patent Office recognizes, and through that recognition, appears to sanction that Applicants will be submitting information that is related to the invention but that does not compel a prima facie case of unpatentability. According to MPEP 2001.05 "if information is not material, there is no duty to disclose the information to the Office. Thus, it is theoretically possible for applicants to draft claims and a specification to avoid a prima facie case of obviousness over a reference and then to be able to withhold the reference from the examiner. The office believes that most applicants will wish to submit the information, however, even though they may not be required to do so, to strengthen the patent and avoid the risks of an incorrect judgment on their part on materiality or that it may be held that there was an intent to deceive the Office." (MPEP 2001.05, emphasis added).

Each of the references cited in the IDS submitted on January 14, 2004 was previously cited to the Patent Office in a prior application relied upon for an earlier filing date under 35 USC 120. Such information is indicated at the end of the Form 1449. According to MPEP2006.06(b) if "the application under examination is identified as a continuation, divisional, or continuation-in-part of an earlier application, the examiner will consider the prior art cited in the earlier application. See MPEP 609. The examiner must indicate in the first Office action whether the prior art in a related application has been reviewed. Accordingly, no separate citation of the same prior art need be made in the later application." (MPEP 2001.06(b)). "The examiner will consider information which has been considered by the Office in a parent application when examining: (A) a continuation application filed under 37 CFR 1.53(b), (B) a divisional application filed under 37 CFR 1.53(b), or

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(C) a continuation-in-part application filed under 37 CFR 1.53(b). A listing of the information need not be resubmitted in the continuing application unless the applicant desires the informatin to be printed on the patent." (MPEP 609.02(A)(2)) In this case, Applicant desires to have it printed on the front page of the patent. Additionally, as stated above, Applicants have submitted herewith a clean copy of the 1449 which is updated with the format requirements now in place under 37 CFR 1.98(a)(1).

Of the 46 US Patent and PreGrant Patent documents listed on the IDS and mentioned by the Examiner as being reviewed and considered to have a "low percentage... material to patentability", 16 are other patents/applications belonging to the same applicant or assignee. According to MPEP 2004 (9) applicants should bring such patents/applications to the attention of the Examiner. "Do not rely on the examiner of a particular application to be aware of other applications belonging to the same applicant or assignee. It is desirable to call such applications to the attention of the examiner even if there is only a question that they might be 'material to patentability' of the application the examiner is considering." (MPEP 2004 (9)).

It is unclear from the rejection which section of 37 CFR 1.56, 1.97, and 1.98 with which Applicants' IDS fails to comply. "multiple information disclosure statements may be filed in a single application, and they will be considered, provided each is in compliance with the appropriate requirements of 37 CFR 1.97 and 37 CFR 1.98." (MPEP 609). Thus, Applicants request that the cited references be reviewed by the Examiner and be granted the date of submission of the original filed IDS.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 23/2825, under Docket No. C1039.70070US00. A duplicate copy of this paper is enclosed.

Dated: March 30, 2007

Docket No. C1039.70079US00

Respectfully submitted,

Helen C. Lockhar

Registration No.: 39,248

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INFORMATION ISCLOSURE STATEMENT BY APPLICANT

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Sheet

APPLICATION NO.: 10/627,413

ATTY. DOCKET NO.: C1039.70079US00

FILING DATE:

July 25, 2003

CONFIRMATION NO.: 3204

APPLICANT:

Arthur M. Krieg, et al.

GROUP ART UNIT: 1648

EXAMINER: Le, Emily M.

U.S. PATENT DOCUMENTS

Examiner's	Cite	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication or of issue of Cited Document	
Initials	No.	Number	Kind Code	Document	MM-DD-YYYY	
	*	3,906,092		Hilleman et al.	09-16-1975	
	*	5,248,670		Draper et al.	09-28-1993	
	*	5,585,479		Hoke et al.	12-17-1996	
- "	*	5,663,153		Hutcherson et al.	09-02-1997	
	*	5,723,335		Hutcherson et al.	03-03-1998	
	*	5,786,189		Locht et al.	07-28-1998	
	*	5,849,719		Carson et al.	12-15-1998	
	*	6,194,388	B1	Krieg et al.	02-27-2001	
	*	6,207,646	B1	Krieg et al.	03-27-2001	
· · -	*	6,214,806	Bl	Krieg et al.	04-10-2001	
-	*	6,218,371	B1	Krieg et al.	04-17-2001	
	*	6,225,292	B1	Raz, et al.	05/01/2001	
	*	6,239,116	B1	Krieg et al.	05-29-2001	
	*	6,339,068	BI	Krieg et al.	01-15-2002	
	*	6,406,705	Bl	Davis et al.	06-18-2002	
	*	6,429,199	B1	Krieg et al.	08-06-2002	
	*	6,498,148	B1	Raz	12/24/2002	
,	*	6,514,948	B1	Raz, et atl	02/04/2003	
	*	6,534,062	B2	Krieg, et al.	03/18/2003	
	*	6,552,006	B2	Raz et al.	04/22/2003	
	*	6,562,798	B1	Schwartz	05/13/2003	
	*	6,589,940	B1	Raz et al.	07/08/2003	
	*	6,610,661	B1	Carson et al.	08/26/2003	
	*	6,653,292	Bl	Krieg et al.	11/25/2003	
	*	US 2001/0046967	A1	Van Nest	11/29/2001	
	*	US 2002/0028784	A1	Van Nest	03/07/2002	
	*	US 2002/0055477	A1	Nest	05/09/2002	
	*	US 2002/0098199	A1	Nest et al.	07/25/2002	
	*	US 2002/0107212	A1	Van Nest et al.	08/08/2002	
	*	US 2002/0142978	A1	Van Nest et al.	10/03/2002	
	*	US 2002/0156033	A1	Raz et al.	10/24/2002	
	*	US 2003/0049266	A1	Bratzler et al.	03/13/2003	
	*	US 2003/0050263	A1	Fearon et al.	03/13/2003	
	*	US 2003/0078223	A1	Krieg et al.	04/24/2003	
	*	US 2003/0092663	A1	Raz et al.	05/15/2003	
	*	US 2003/0109469	A1	Raz	06/12/2003	
	*	US 2003/0119773	A1	Carson et al.	06/26/2003	

* US 2003/0129251 A1 Raz et al. 07/10/2003



FORM PTC)-1449/A and B (M	lodifie	d)	APPLICATION NO.:	10/627,413	ATTY. DOCKET NO.: C1039.70079US00
	RMATION D			FILING DATE:	July 25, 2003	CONFIRMATION NO.: 3204
STAT	EMENT BY	APP	PLICANT	APPLICANT:	Arthur M. Krieg, et	al.
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U.S. PATENT DOCUMENTS

Examiner's Initials	Cite No.	U.S. Patent Document	Nam	e of Patentee or Applicant of Cited Document	Date of Publication or of issue of Cited Document MM-DD-YYYY
	*	US 2003/0133988	A1	Van Nest et al.	07/17/2003
	*	US 2003/0143213	A1	Fearon et al.	07/31/2003
	*	US 2003/0147870	A1	Raz et al.	08/07/2003
	*	US 2003/0175731	A1	Raz et al.	09/18/2003
	*	US 2003/0186921	A1	Rearon et al	10/02/2003
	*	US 2003/0199466	Al	Fearon et al.	10-23-2003
	*	US 2003/0212028	Al	Raz et al.	11-13-2003
	*	US 2003/0216340	A1	Van Nest et al.	11-20-2003

FOREIGN PATENT DOCUMENTS

Examiner's	Cite	For	eign Patent Docum	nent	Name of Patentee or Applicant of Cited Document	Date of Publication of	Translation
Initials	No.	Office/ Country	Number	Kind Code	(not necessary)	Cited Document MM-DD-YYYY	(Y/N)
	*	GB	2216416A		Sandoz, Ltd.	11-10-1989	
	*	WO	91/12811		ISIS Pharmaceuticals Inc.	09-05-1991	
	*	EPO	0468520 A3		Mitsui Toatsu Chemicals, Inc.	01-29-1992	
	*	wo	92/03456		ISIS Pharmaceuticals, Inc.	03-05-1992	
	*	WO	92/18522		The Salk Institute for Biological Studies	10-29-1992	
	*	WO	92/21353		Genta Incorporated	12-10-1992	
	*	EPO	0302758 81		New England Medical Center Hospitals, Inc.	03-16-1994	
	*	WO	94/19945		ISIS Pharmaceuticals Inc.	09-15-1994	
	*	WO	95/05853		Regents of the University of CA	03-02-1995	
	*	WO	95/26204		ISIS Pharmaceuticals Inc.	10-05-1995	
	*	WO	96/02555		University of Iowa Research Foundation	02-01-1996	
	*	WO	96/35782		Applied Research Systems	11-14-1996	
	*	WO	97/28259		Regents of the University of California	08-07-1997	
	*	wo	98/14210		Regents of the University of California	04-09-1998	
-	*	WO	98/16247	;	Regents of the University of CA	04-231998	
	*	WO	98/18810		University of Iowa Research Foundation	05-07-1998	
	*	WO	98/32462	Al	Wagner et al.	07-30-1998	
	*	WO	98/37919		University of Iowa Research Foundation	09-03-1998	
	*	WO	98/40100		Ottawa Civic Loeb Research Institute	09-17-1998	
	*	WO	98/52581		Ottawa Civic Loeb Research Institute	11-26-1998	
	*	WO	98/55495	A2	Dynavax Tech. Corp.	03/11/1998	
	*	WO	99/11275	A2	Regents of the University of CA	03-11-1999	
	*	WO	99/62923	A2	Dynavax Tech. Corp	12/09/1999	
	*	WO	00/20039	A1	Regents of the University of CA	04/13/2000	

FORM PTC	0-1449/A and B (M	Iodifie	d)	APPLICATION NO.:	10/627,413	ATTY. DOCKET NO.: C1039.70079US00
	RMATION D			FILING DATE:	July 25, 2003	CONFIRMATION NO.: 3204
STAT	EMENT BY	APP	PLICANT	APPLICANT:	Arthur M. Krieg, et	al.
				GROUP ART UNIT:	1648	EXAMINER: Le, Emily M.
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FOREIGN PATENT DOCUMENTS

Examiner's Initials	Cite No.	Foreign Patent Document		nent	Name of Patentee or Applicant of Cited Document (not necessary)	Date of Publication of Cited Document MM-DD-YYYY	Translation (Y/N)
	*	WO	00/21556	A1	Dynavax Tech Corp.	04/20/2000	
	*	WO	00/62781	Al	Regents of the University of CA	10/26/2000	
	*	WO	01/02007	A 1	The Reagents of the Univ. of California	01-11-2001	
	*	WO	01/12804	A2	Hybridon, Inc.	02-22-2001	
	*	WO	01/12223	A2	Dynavax Tech. Corp.	02-22-2001	
	*	WO	01/55341	A2	The Reagents of the Univ. of California	08-02-2001	
	*	WO	01/68117	A2	Dynavax Tech. Corp.	09-20-2001	
	*	WO	01/68116	A2	Dynavax Tech. Corp.	09-20-2001	
	*	WO	01/68078	A2	Dynavax Tech. Corp.	09-20-2001	
	*	WO	01/68077	A2	Dynavax Tech. Corp.	09-20-2001	
	*	WO	01/68103	A2	Dynavax Tech. Corp.	09-20-2001	

Cite	Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item	Translation
No	(book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s), publisher, city and/or country where published.	(Y/N)
*		
*		
		.
*		
*	ANGIER, N., Microbe DNA Seen as Alien By Immune System, New York Times, 4/11/95.	
*	AZAD RF et al., Antiviral Activity of a Phosphorothioate Oligonucleotide Complementary to RNA	
	of the Human Cytomegalovirus Major Immediate-Early Region, Antimicrobial Agents and	
*		
	Kekkaku, (1992) Vol. 69, 9:45-55.	
*	BALLAS ZK et al., Induction of NK activity in murine and human cells by CpG motifs in	
	oligodeoxynucleotides and bacterial DNA. J Immunol (1996) 157(5):1840-5.	
*	BAYEVER, E., Systemic Administration of a Phosphorothioate Oligonucleotide with a Sequence	
1	Complementary to p53 for Acute Myelogenous leukemia and Myelodysplastic Syndrome: Initial	
	Results of a Phase I Trial, Antisense Res. & Dev. (1993), 3:383-390.	1
*	BENNETT RM et al., DNA binding to human leukocytes. Evidence for a receptor-mediated	
	association, internalization, and degradation of DNA. (1985) J Clin Invest 76(6):2182-90.	
*	BERG DJ et al., Interleukin-10 is a central regulator of the response to LPS in murine models of	
	endotoxic shock and the Shwartzman reaction but not endotoxin tolerance. J Clin Invest (1995)	
	96(5):2339-47.	
*	BLANCHARD DK et al., Interferon-gamma induction by lipopolysaccharide: dependence on	
		1
*		-
	* * * * * * *	(book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s), publisher, city and/or country where published. * ADYA N et al., Expansion of CREB's DNA recognition specificity by Tax results from interaction with Ala-Ala-Arg at positions 282-284 near the conserved DNA-binding domain of CREB. Proc Natl Acad Sci USA (1994) 91(12):5642-6. * AGRAWAL, et al., Pharmacokinetics of Antisense Oligonucleotides, Clin. Pharmacokinet (1995) 28(1):7. * ANDERSON, G., et al. "TH2 and 'TH2-like' cells in allergy and asthma; pharmacological perspectives", TiPS, 15:324-332, (1994) * ANGIER, N., Microbe DNA Seen as Alien By Immune System, New York Times, 4/11/95. * AZAD RF et al., Antiviral Activity of a Phosphorothioate Oligonucleotide Complementary to RNA of the Human Cytomegalovirus Major Immediate-Early Region, Antimicrobial Agents and Chemotherapy, 37:1945-1954, September, 1993. * AZUMA, Biochemical and Immunological Studies on Cellular Components of Tubercle Bacilli, Kekakaku, (1992) Vol. 69, 9:45-55. * BALLAS ZK et al., Induction of NK activity in murine and human cells by CpG motifs in oligodeoxynucleotides and bacterial DNA. J Immunol (1996) 157(5):1840-5. * BAYEVER, E., Systemic Administration of a Phosphorothioate Oligonucleotide with a Sequence Complementary to p53 for Acute Myelogenous leukemia and Myelodysplastic Syndrome: Initial Results of a Phase I Trial, Antisense Res. & Dev. (1993), 3:383-390. * BENNETT RM et al., DNA binding to human leukocytes. Evidence for a receptor-mediated association, internalization, and degradation of DNA. (1985) J Clin Invest 76(6):2182-90. * BERG DJ et al., Interleukin-10 is a central regulator of the response to LPS in murine models of endotoxic shock and the Shwartzman reaction but not endotoxin tolerance. J Clin Invest (1995) 96(5):2339-47. * BLANCHARD DK et al., Interferon-gamma induction by lipopolysaccharide: dependence on interleukin 2 and macrophages. J Immunol (1986) 136(3):963-70.

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FORM PTO	0-1449/A and B (M	lodifie	d)	APPLICATION NO.:	10/627,413	ATTY. DOCKET NO.: C1039.70079US00
	RMATION E			FILING DATE:	July 25, 2003	CONFIRMATION NO.: 3204
STAT	EMENT BY	APP	LICANT	APPLICANT:	Arthur M. Krieg, et	al.
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	· · · · · ·	OTHER ART — NON PATENT LITERATURE DOCUMENTS	
Examiner's Initials	Cite No	Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s),	Translation (Y/N)
	*	publisher, city and/or country where published.	1
	*	BOGGS RT et al., Characterization and modulation of immune stimulation by modified	
	ļ <u></u>	oligonucleotides. Antisense Nucleic Acid Drug Dev (1997) 7(5):461-71.	<u> </u>
	*	BRANDA et al., Immune Stimulation by an Antisense Oligomer Complementary to the rev gene of	
	ļ	HIV-1, Biochemical Pharmacology, (1993) Vol. 45, 10:2037-2043.	
	*	BRANDA RF et al., Amplification of antibody production by phosphorothioate	
		oligodeoxynucleotides, J. Lab Clin Med (1996) 128(3):329-38.	
	*	BRISKIN M et al., Lipopolysaccharide-unresponsive mutant pre-B-cell lines blocked in NF-kappa B	
		activation, (1990) Mol Cell Biol 10(1):422-5.	
	*	CHACE, J. et al., Regulation of Differentiation in CD5+ and Conventional B Cells, Clinical	1 1
		Immunology and Immunopathology, (1993) 68:3:327-332.	
	*	CHANG YN et al., The palindromic series I repeats in the simian cytomegalovirus major immediate-	
		early promoter behave as both strong basal enhancers and cyclic AMP response elements, J Virol	
		(1990) 64(1):264-77.	
	*	CHU RS et al., CpG oligodeoxynucleotides act as adjuvants that switch on T helper 1 (Th1)	
		immunity, (1997) J Exp Med 186(10):1623-31	
	*	COSSUM et al., Pharmacokinetics of a 14C-Labeled Phosphorothioate Oligonucleotide, ISIS 2105,	
		after Intradermal Administration to Rats, J Pharmacol Exp Therapeutics (1993) 269(1):89.	
	*	COWDERY JS et al., Bacterial DNA induces NK cells to produce IFN-gamma in vivo and increases	
		the toxicity of lipopolysaccharides, <i>J Immunol</i> (1996) 156(12):4570-5.	
	*	CROSBY et al., The Early Responses Gene FGFI-C Encodes a Zinc Finger Transcriptional Activator	
		and is a Member of the GCGGGGGCG (GSG) Element-Binding Protein Family, Mol. Cell. Biol.]
		(1991) 2:3835-3841.	
	*	CRYSTAL, Transfer of Genes to Humans: Early Lessons and Obstacles to Success. Science, (1995)	
	1	Vol. 270, pp. 404-410.	1
	*	D'ANDREA A et al., Interleukin 10 (IL-10) inhibits human lymphocyte interferon	
		gamma-production by suppressing natural killer cell stimulatory factor/IL-12 synthesis in accessory	
		cells, J Exp Med (1993) 178(3):1041-8.	
	*	ELKINS, K. L., Rhinehart-Jones, T. R., et al., "Bacterial DNA containing CpG motifs stimulates	
		lymphocyte-dependent protection of mice against lethal infection with intracellular bacteria." J	1
		Immunol 162:2291-2298, 1999.	
	*	ENGLISCH et al., Chemically Modified Oligonucleotides as Probes and Inhibitors, Angew. Chem.	
		Int. Ed. Engl (1991) 30:613-629.	
	*	ERB KJ et al., Infection of mice with Mycobacterium bovis-Bacillus Calmette-Guerin (BCG)	
		suppresses allergen- induced airway eosinophilia, J Exp Med (1998) 187(4):561-9]
	*	ETLINJER, Carrier sequence selection - one key to successful vaccines, <i>Immunology Today</i> , (1992)	
		Vol. 13, 2:52-55.	
	*	FOX RI, Mechanism of action of hydroxychloroquine as an antirheumatic drug. Chemical Abstracts,	
		(1994) 120:15, Abstract No. 182630.	
	*	FREIDAG, B. L et al., "CpG oligodeoxynucleotides and interleukin-12 improve the efficacy of	
	}	Mycobacterium bovis BCG vaccination in mice challenged with M. tuberculosis.: Infect Immun	
		68:2948-2953, (2000).	
	*	GAO, W-Y et al., Phosphorothioate oligonucleotides are inhibitors of human DNA polymerases and	
		Rnase H: Implications for antisense technology. Mol. Pharmacol. (1992), 41, 223-229.	
	*	GURA, T., Antisense Has Growing Pains. Science (1995), 270:575-576.	
	*	HADDEN J et al., Immunopharmacology, <i>JAMA</i> , (1992) 268:20:2964-2969.	1

FORM PTO	0-1449/A and B (M	Iodifie	d)	APPLICATION NO.:	10/627,413	ATTY. DOCKET NO.: C1039.70079US00
	RMATION D			FILING DATE:	July 25, 2003	CONFIRMATION NO.: 3204
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Examiner's	Cite	Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item	Translatio
Initials	No	(book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s),	(Y/N)
ilitiais	140	publisher, city and/or country where published.	(1/14)
	*	HADDEN J et al., Immunostimulants. TIPS, (1993), 141:169-174.	
	*	HALPERN MD et al., Bacterial DNA induces murine interferon-gamma production by stimulation of	.
		interleukin-12 and tumor necrosis factor-alpha. Cell Immunol (1996) 167(1):72-8.	
	*	HATZFELD J., Release of Early Human Hematopoietic Progenitors from Quiescence by Antisense	
	-	Transforming Growth Factor β1 or Rb Oligonucleotides, J. Exp. Med., (1991) 174:925-929.	
	*	HAYASHI, T.et al., "Enhancement of innate immunity against Mycobacterium avium infection by	
		immunostimulatory DNA is mediated by indoleamine 2,3-dioxygenase." <i>Infect Immun</i> 69:6156-	
		6164, (2001).	
	*	d	
	*	HIGHFIELD PE, Sepsis: the More, the Murkier. Biotechnology, (1994) 12:828.	
	*	HOEFFLER JP et al., Identification of multiple nuclear factors that interact with cyclic adenosine	
		3',5'-monophosphate response element-binding protein and activating transcription factor-2 by	
		protein-protein interactions., (1994) Mol Endocrinol 5(2):256-66.]
•	*	HORSPOOL JH et al., Nucleic acid vaccine-induced immune responses require CD28 costimulation	1
		and are regulated by CTLA4. (1998) J. Immunol, 160, 2706-2714.	
	*	IGUCHI-ARIGA SM and Shaffner W, CpG methylation of the cAMP-responsive enhancer/promoter	
	1		
		sequence TGACGTCA abolishes specific factor binding as well as transcriptional activation. Genes	1
	ļ—.	Dev (1989) 3(5):612-9.	
	*	ISHIKAWA R et al., IFN induction and associated changes in splenic leukocyte distribution. J	
		Immunol (1993) 150(9):3713-27.	
	*	IVERSON, P., et al., "Pharmacokinetics of an Antisense Phosphorothioate Oligodeoxynucleotide	
		against rev from Human Immunodeficiency Virus Type 1 in the Adult male Rate Following Single	
	 	Injections and Continuous Infusion", Antisense Research and Development, (1994) 4:43-52.	
	*	JAKWAY JP et al., Growth regulation of the B lymphoma cell line WEHI-231 by	1
		anti-immunoglobulin, lipopolysaccharide, and other bacterial products. J Immunol (1986)	
		137(7):2225-31.	
	*	JAROSZEWSKI JW and Cohen JS, Cellular uptake of antisense oligonucleotides. Adv Drug	
		Delivery Rev (1991) 6(3):235-50.	
	*	JONES TR et al., Synthetic oligonucleotides containing CpG motifs enhance immunogenicity of a	
		peptide malaria vaccine in Aotus monkeys. Vaccine (1999) 17, 3065-3071.	
	*	JUFFERMANS, N. P. et al., "CpG oligodeoxynucleotides enhance host defense during murine	
•		tuberculosis." Infect Immun 70:147-152, (2002).	1 1
	*	KATAOKA, T. et al., Antitumor Activity of Synthetic Oligonucleotides with Sequences from cDNA	
	•	Encoding Proteins of Mycobacterium bovis BCG, JPN. J. Cancer Res. (1992) 83:244.	
	*		-
	1	KAWANO, K., et al., "Analysis and Regulation of interferon-gamma production by peripheral blood	1 1
		lymphocytes from patients with bronchial asthma", ABSTRACT, Arerugi, 43:3:482-91, (1994)	
	*	KIMURA Y et al., Binding of Oligoguanylate to Scavenger Receptors Is Required for	ļ l
		Oligonucleotides to Augment NK Cell Activity and Induce IFN, J. Biochem., (1994) Vol. 116, 5:991-	1
		994.	
	*	KLINE JN et al., CpG motif oligonucleotides are effective in prevention of eosinophilic	
	1	inflammation in a murine model of asthma. J Invest Med (1996) 44(7):380A.	
	*	KLINE JN et al., CpG oligonucleotides can reverse as well as prevent Th2-mediated inflammation in	
	1	a murine model of asthma. J Invest Med (1997) 45(7):298A.	
	*	KLINE JN et al.,"Immune redirection by CpG oligonucleotides. Conversion of a Th2 response to a	
	1		
	l	Th1 response in murine model of asthma." J. Invest Med. 45(3):282A, 1997.	L

FORM PTO-1449/A and B (Modified)				APPLICATION NO.:	10/627,413	ATTY. DOCKET NO.: C1039.70079US00
	RMATION D			FILING DATE:	July 25, 2003	CONFIRMATION NO.: 3204
STATEMENT BY APPLICANT			APPLICANT:	Arthur M. Krieg, et	al.	
				GROUP ART UNIT:	16/18	EXAMINER: Le, Emily M.
Sheet	6	of	10	GROOF ART UNIT.	1070	DAAWINDA. De, Emily W.

Examiner's	Cite	Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item	Translatio	
Initials	No	(book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s),	(Y/N)	
		publisher, city and/or country where published.	, ,	
	*	KLINMAN DM et al., CpG motifs present in bacteria DNA rapidly induce lymphocytes to secrete		
	<u> </u>	interleukin 6, interleukin 12, and interferon gamma. Proc Natl Acad Sci USA (1996) 93(7):2879-83.		
	*	KLINMAN, D. et al., Immune Recognition of Foreign DNA: A Cure for Bioterrorism?, Immunity		
		(1999) 11:123.		
	*	KLINMAN, D. M. et al., "Repeated administration of synthetic oligodeoxynucleotides expressing		
		CpG motifs provides long-term protection against bacterial infection. <i>Infect Immun</i> 67:5658-5663,		
		1999"		
	*	KLINMAN, D. M., Kamstrup, S., Verthelyi, D., Gursel, I., Ishii, K. J., Takeshita, F., and Gursel, M.		
		Activation of the innate immune system by CpG oligodeoxynucleotides: immunoprotective activity		
		and safety. Springer Semin Immunopathol 22:173-183, 2000		
•	*	KRIEG, A. M., et al., "CpG DNA induces sustained IL-12 expression in vivo and resistance to		
	j	Listeria monocytogenes challenge." J Immunol 161:2428-2434, 1998.		
	*	KRIEG, CpG Motifs in Bacterial DNA and Their Immune Effects, Annu. Rev. Immunol. (2002)		_
		20:709		
	*	KRIEG AM el al, A Role for Endogenous Retroviral Sequences in the Regulation of Lymphocyte		
		Activation, Journal of Immunology, Vol. 143, 2448-2451 (1989)		
	*	KRIEG AM et al, The role of CpG dinuleotides in DNA vaccines, Trends in Microbiology, Vol. 6,		
		pp. 23-27, Jan 1998.		
	*	KRIEG AM et al, Phosphorothioate Oligodeoxynucleotides: Antisense or Anti-Protein?, Antisense		
		Research and Development, (1995), 5:241		
	*	KRIEG AM et al., CpG DNA: A Pathogenic Factor in Systemic Lupus Erythematosus?, Journal of	1 .	,
		Clinical Immunology, (1995) 15:6:284-292	1	
	*	KRIEG AM et al., CpG motifs in bacterial DNA trigger direct B-cell activation. <i>Nature</i> 374:546-9,		
		1995.		
	*	KRIEG AM et al., Leukocyte Stimulation by Oligodeoxynucleotides, Applied Antisense		
		Oligonucleotide Technology, (1998), 431-448		
	*	KRIEG AM et al., Modification of antisense phosphodiester oligodeoxynucleotides by a 5'		
		cholesteryl moiety increases cellular association and improves efficacy, <i>Proc. Natl. Acad. Sci.</i> ,		
		(1993), 90:1048-1052.		
	*	KRIEG AM et al., Oligodeoxynucleotide modifications determine the magnitude of B cell		
	-	stimulation by CpG motifs. Antisense Nucleic Acid Drug Dev (1996) 6(2):133-9.		
	*	KRIEG AM et al., Uptake of oligodeoxyribonucleotides by lymphoid cells is heterogeneous and		_
		inducible. Antisense Res Dev (1991) 1(2):161-71.		
	*	KRIEG AM, An innate immune defense mechanism based on the recognition of CpG motifs in		
		microbial DNA. J Lab Clin Med (1996) 128(2):128-33.		
	*	KURAMOTO et al., Oligonucleotide Sequences Required for Natural Killer Cell Activation, Jpn. J.		
		Cancer Res., (1992) 83:1128-1131.		
	*	LEONARD et al., Conformation of Guanine 8-Oxoadenine Base Pairs in the Crystal Structure of		
		d(CGCGAATT(08A)GCG), Biochemistry (1992) 31(36):8415-8420.		
	*	LIPFORD, G. B. et al. "Immunostimulatory DNA: sequence-dependent production of potentially		
		harmful or useful cytokines." Eur J Immunol 27:3420-3426, 1997.		
	*	MACFARLANE DE and Manzel L, Antagonism of immunostimulatory CpG-oligodeoxynucleotides by		
	 	quinacrine, chloroquine, and structurally related compounds. <i>J Immunol</i> (1998) 160(3):1122-31.		
	*	MANZEL L and Macfarlane DE, Lack of Immune Stimulation by Immobilized CpG-oligonucleotide. Antisense		
	<u> </u>	& Nucleic Acid Drug Development, (1999) 459-464.	1	

FORM PTC)-1449/A and B (M	lodifie	i)	APPLICATION NO.:	10/627,413	ATTY. DOCKET NO.: C1039.70079US00
	RMATION D			FILING DATE:	July 25, 2003	CONFIRMATION NO.: 3204
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Examiner's	7 0:4	OTHER ART — NON PATENT LITERATURE DOCUMENTS	T. 1.41
Initials	Cite No	Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s), publisher, city and/or country where published.	Translation (Y/N)
	*	MASTRANGELO MJ et al., Gene therapy for human cancer: an essay for clinicians. Seminars in Oncology (1996) 23(1):4-21.	
	*	MATSON S and Krieg AM, Nonspecific suppression of [3H]thymidine incorporation by "control" oligonucleotides. <i>Antisense Res Dev</i> (1992) 2(4):325-30.	
	*	MCINTYRE KW et al., A sense phosphorothioate oligonucleotide directed to the initiation codon of transcription factor NF-kappa B p65 causes sequence-specific immune stimulation. <i>Antisense Res Dev</i> (1993) 3(4):309-22.	
	*	MESSINA et al., Stimulation of <i>in vitro</i> Murine Lymphocyte Proliferation by Bacterial DNA. <i>J. Immunol.</i> , (1991) Vol. 147, 6:1759-1764.	
	*	MESSINA et al., The Influence of DNA Structure on the <i>in vitro</i> Stimulation of Murine Lymphocytes by Natural and Synthetic Polynucleotide Antigens. <i>Cellular Immunology</i> , (1993) 147:148-157.	
	*	MOJCIK, C., et al., Administration of a Phosphorothioate Oligonucleotide Antisense Murine Endogenous Retroviral MCF env Causes Immune Effect in vivo in a Sequence-Specific Manner, Clinical Immunology and Immunopathology, (1993) 67:2:130-136.	
	*	MOTTRAM et al., A novel CDC2-related protein kinase from leishmania mexicana LmmCRK1 is post-translationally regulated during the life cycle. <i>J. Biol. Chem.</i> (1993) 268:28, 21044-21052.	
	*	New England BIOLABS 1988-1989 Catalog	
	*	NYCE JW and Metzger WJ, DNA antisense therapy for asthma in an animal model. <i>Nature</i> (1997) 385:721-725.	
	*	PISETSKY DS, The immunologic properties of DNA. J Immunol (1996) 156(2):421-3.	
	*	PISETSKY et al., Stimulation of Murine Lymphocyte Proliferation by a Phosphorothioate Oligonucleotide with Antisense Activity for Herpes Simplex Virus. <i>Life Science</i> ,(1994) Vol. 54, pp. 101-107.	·
	*	PISETSKY, D., "Stimulation of in vitro proliferation of murine lymphocytes by synthetic oligodeoxynucleotides", <i>Molecular Biology Repairs</i> , (1993) 18:217-221.	
	*	PISETSKY, Immunological Consequences of Nucleic Acid Therapy, Antisense Research and Development, (1995) 5:219-225.	
	*	RAZ E et al., Preferential induction of a Th1 immune response and inhibition of specific IgE antibody formation by plasmid DNA immunization. <i>Proc Natl Acad Sci USA</i> (1996) 93(10):5141-5.	
	*	RICCI, M., et al., "T cells, cytokines, IgE and allergic airways inflammation", <i>J invest Allergol Clin Immunol</i> ", 4:5;214-220, (1994)	
	*	ROMAN M et al., Immunostimulatory DNA sequences function as T helper-1-promoting adjuvants. Nat Med (1997) 3(8):849-54.	
	*	SATO et al., Immunostimulatory DNA Sequences Necessary for Effective Intradermal Gene Immunization, <i>Science</i> , (1996) Vol. 273, pp. 352-354.	
	*	SCHNELL et al., Identification and characterization of a Saccharomyces cerevisiae gene (PAR1) conferring resistance to iron chelators. <i>Eur. J. Biochem.</i> , 200:487-493.	
	*	SCHWARTZ DA et al., CpG motifs in bacterial DNA cause inflammation in the lower respiratory tract. <i>J Clin Invest</i> (1997) 100(1):68-73.	
	*	SCHWARTZ DA et al., Endotoxin responsiveness and grain dust-induced inflammation in the lower respiratory tract. <i>Am J Physiol</i> (1994) 267(5 Pt 1):L609-17.	
	*	SCHWARTZ DA et al., The role of endotoxin in grain dust-induced lung disease. Am J Respir Crit Care Med (1995) 152(2):603-8	

FORM PTC	0-1449/A and B (M	lodifie	d)	APPLICATION NO.:	10/627,413	ATTY. DOCKET NO.: C1039.70079US00
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Initials	No	(book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s),	(Y/N)
ilitiais	NO	publisher, city and/or country where published.	[(1/14)
	*	SEDEGAH, M.et al. "Interleukin 12 induction of interferon g-dependent protection against malaria."	
	*		1
		Proc Natl Acad Sci U S A 91:10700-10702, 1994.	
	*	SETHI, S. et al. "Postexposure prophylaxis against prion disease with a stimulator of innate	
	ļ	immunity." Lancet 360:229-230, 2002.	
	*	SHIRAKAWA T et al., The inverse association between tuberculin responses and atopic disorder.	
		Science (1997) 275(5296):77-9.	
	*	SPARWASSER T et al., Macrophages sense pathogens via DNA motifs: induction of tumor necrosis	
		factor-alpha-mediated shock. Eur J Immunol (1997) 27(7):1671-9.	ļ į
	*	SPIEGELBERG, H., et al., "Recognition of T Cell Epitopes and Lymphokine Secretion by Rye Grass	
		Allergen Lolium perenne I-Specific Human T Cell Clones", J of Immunology, 4706-4711, (1994)	
** **	*	STACEY, K. J et al. "Immunostimulatory DNA as an adjuvant in vaccination against Leishmania	
		major." Infect Immun 67:3719-3726, 1999.	
	*	STEIN CA et al., Oligonucleotides as inhibitors of gene expression: a review. Cancer Research,	
	"		
	 	(1988) 48:2659-2668.	
	*	STULL et al., Antigene, Ribozyme, and Aptamer Nucleic Acid Drugs: Progress and Prospects,	·
		Pharmaceutical Res., (1995) Vol. 12, 4:465-483.	ļ
	*	SUBRAMANIAN et al., Theoretical Considerations on the "Spine of Hydration" in the Minor	ļ į
		Groove of d(CGCGAATTCGCG) d(GCGCTTAAGCGC): Monte Carlo Computer Simulation.	1
		Proc. Nat'l. Acad. Sci. USA, (1988) 85:1836-1840.	
	*	TANAKA T et al., An antisense Oligonucleotide complementary to a sequence in IG2b increases	
		G2b germline transcripts stimulates B cell DNA synthesis and inhibits immunoglobulin secretion. J.	
		Exp. Med., (1992) 175:597-607.	
	*	THORNE PS., Experimental grain dust atmospheres generated by wet and dry aerosolization	
		techniques. Am J Ind Med (1994) 25(1):109-12.	
	*	TOKUNAGA T et al., A synthetic single-stranded DNA, poly(dG,dC), induces interferon-alpha/beta	1
	"	and -gamma, augments natural killer activity, and suppresses tumor growth. Jpn J Cancer Res (1988)	
			1 1
		Jun;79(6):682-6.	+
	*	TOKUNAGA T et al., Synthetic Oligonucleotides with Particular Base Sequences form the cDNA	
		Encoding Proteins of Myobacterium bovis BCG Induce Interferons and Activate Natural Killer Cells,	
		Microbiol. Immunol., (1992) Vol. 36, 1:55-66.	
	*	UHLMANN et al., Antisense Oligonucleotides: A New Therapeutic Principle. Chemical Reviews,	
		(1990) 90:543-584.	
	*	WAGNER RW, Gene inhibition using antisense oligodeoxynucleotides. Nature, (1994) 372:L333-	
		335.	
	*	WALKER, P. S. et al. "Immunostimulatory oligodeoxynucleotides promote protective immunity and	
		provide systemic therapy for leishmaniasis via IL-12- and IFN-g-dependent mechanisms." <i>Proc Natl</i>	
		Acad Sci U S A 96:6970-6975, 1999.	
	*	WALKER, C., et al., "Activated T Cells and Cytokines in Bronchoalveolar Lavages from Patients	
	1	with Various Lung Diseases Associated with Eosinophilia", Am J Respir Crit Care Med, 150:1038-	
		1048, (1994)	
	*	WALLACE et al., Oligonucleotide probes for the screening of recombinant DNA libraries. <i>Methods</i>	+
	1		
	+	in Enzymology, (1987) 152:432-442.	+
	*	WEISS R., Upping the Antisense Ante: Scientists bet on profits from reverse genetics. Science,	
		(1991) 139:108-109.	1

FORM PTC)-1449/A and B (M	Iodifie	d)	APPLICATION NO.:	10/627,413	ATTY. DOCKET NO.: C1039.70079US00
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97)89:2994-2998.	
l. Chem., (1988)	
n. Pharmaceutical	
g a Palindromic	
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cobacterium bovis	
otides are Required to	
(1992) Vol. 148,	
Mycobacterium bovis	
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		publisher, city and/or country where published.		_
	*	ZIMMERMANN, S. et al., "CpG oligodeoxynucleotides trigger protective and curative Th1		٦
		responses in lethal murine leishmaniasis." J Immunol 160:3627-3630, 1998.		

EXAMINER	DATE CONSIDERED

#EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

^{*}a copy of this reference is not provided as it was previously cited by or submitted to the office in one of the following prior applications, Serial No. 08/386.063, filed 02/07/95, Serial No. 08/738,652, filed 10/30/96, Serial No. 08/960.774, filed 10/30/97, Serial No. 09/630,319, filed 10/30/96, or Serial No. 10/187,489, filed 10/2002 relied upon for an earlier filing date under 35 U.S.C. 120 (continuation-in-part, and divisional applications).